Association between fish consumption, long chain omega 3 fatty acids, and risk of cerebrovascular disease: systematic review and meta-analysis


CRD summary
This generally well-conducted review concluded that high fish consumption was significantly associated with a reduced risk of cerebrovascular disease, but long-chain omega-3 fatty acid supplements were not. The beneficial effects of fish might come from a wide range of nutrients found in them. The conclusions are likely to be reliable.

Authors' objectives
To clarify the associations between the consumption of fish, long-chain omega-3 fatty acids, and the risk of cerebrovascular disease, in primary and secondary prevention.

Searching
MEDLINE, EMBASE, BIOSIS Previews, and Science Citation Index were searched, without language restrictions, to September 2012. Reference lists of retrieved studies were searched. The search strategies were reported in an online appendix.

Study selection
Randomised controlled trials (RCTs) were eligible for inclusion if they assessed the effects of long-chain omega-3 fatty acid supplements or fish or seafood consumption in adults and reported cerebrovascular disease endpoints. Prospective cohort studies were eligible if they investigated the associations between the consumption of fish or seafood or long-chain omega-3 fatty acids, or circulating omega-3 fatty acid levels and cerebrovascular disease, in the general population or people at a high risk of cardiovascular disease. Primary and secondary prevention studies were eligible. Studies had to have at least one year of follow-up.

Most studies were conducted in the USA, western Europe, or Japan. They were published between 1989 and 2012. All the cohort studies were conducted in the general population, and all the RCTs were in at-risk groups. Almost two thirds of studies recruited men and women, some recruited men only, and a few recruited women only. Where reported the age of participants ranged from 16 to 98 years.

Two independent reviewers selected studies for the review; disagreements were resolved through consensus or referral to a third reviewer.

Assessment of study quality
Two independent reviewers assessed study quality using criteria based on the Meta-analysis Of Observational Studies in Epidemiology (MOOSE), the Quality Assessment Tool for Systematic reviews of Observational studies (QATSO), and the Strengthening the Reporting of Observational studies in Epidemiology (STROBE). These assessed the provision of a study rationale, appropriate selection criteria, a validated questionnaire or assay, blinding, whether the outcomes measured were self-reported, and adjustment for confounders. Studies were given a score out of six.

Data extraction
Two independent reviewers extracted the incidence of cerebrovascular events from the RCTs. These data were used to calculate relative risks and 95% confidence intervals. To enable comparisons within each cohort study, the risk estimates were transformed to compare the top and bottom third of the population's baseline distribution of exposure values (the method was reported). Hazard and odds ratios were assumed to approximate the same measure as relative risks. Where studies reported results with differing degrees of confounder adjustment, the maximum adjusted estimate was used.

Methods of synthesis
Pooled relative risks and 95% confidence intervals were calculated using a random-effects model. Heterogeneity was investigated using $X^2$ and $I^2$. A dose-response (number of servings over a given time period) for fish consumption was
investigated. Meta-regression was used to investigate the impact of study-level characteristics (no details were given). Publication bias was assessed using funnel plots and the Egger test.

Results of the review
Thirty-eight studies (45 articles) were included in the review (794,000 participants); 26 were cohort studies and 12 were RCTs. The average follow-up ranged from one to 30 years. Nineteen studies scored six out of six, 16 scored five, and the remainder scored four, on the quality assessment.

The risk of cerebrovascular disease was reduced with two to four servings (RR 0.94, 95% CI 0.90 to 0.98; I²=22%; 18 cohort studies) and five or more servings (RR 0.88, 95% CI 0.81 to 0.96; I²=20%; eight cohort studies) of fish or seafood, compared with one or less serving per week. There was no significant effect of long-chain omega-3 fatty acid supplements on cerebrovascular risk (RR 1.03, 95% CI 0.94 to 1.12; I²=3.5%; 12 RCTs); this remained the case when primary and secondary prevention trials were analysed separately. There was no significant association between the risk of cerebrovascular disease and long-chain omega-3 fatty acids measured by circulating biomarkers (four cohort studies) or by self-reported dietary exposure (10 cohort studies).

A wide range of results from subgroup analyses was presented. Results comparing the upper and lower third for within-study comparisons of the cohort studies were reported. There was no evidence of publication bias.

Authors' conclusions
High fish consumption was moderately, significantly associated with a reduced incidence of cerebrovascular disease, but dietary circulating biomarkers and supplements of long-chain omega-3 fatty acids were not significantly associated with the risk of disease. The beneficial effects of eating fish on cerebrovascular risk might be mediated through a wide range of nutrients found in fish.

CRD commentary
The review addressed a clear research question with reproducible inclusion criteria. Relevant sources were searched, without language restrictions, but unpublished studies were not sought. Each stage of the review process was conducted in duplicate, reducing the risk of error and bias. Appropriate criteria were used to assess quality, but some areas of potential bias were not assessed and quality was not fully explored. Only a summary score was presented for each study, making it unclear which bias any study was open to. The assumption that hazard and odds ratios were the same as relative risks, in this case, was appropriate, as the prevalence of the outcomes measured seems to have been sufficiently low. Appropriate methods of synthesis were used and heterogeneity was extensively explored.

This was generally a well-conducted review, with a large number of studies and overall population, and the conclusions are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that their findings supported dietary guidelines that encouraged fish consumption for all and increased intake of fish oils, preferably from oily fish, for people with or at a high risk of coronary heart disease. They proposed that the future guidelines should be principally food based.

Research: The authors stated that data from adequately powered trials were needed to investigate the apparent higher risk of cerebrovascular disease observed in the secondary prevention trials of long-chain omega-3 fatty acid supplements, and potential gender differences in observational studies.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.